



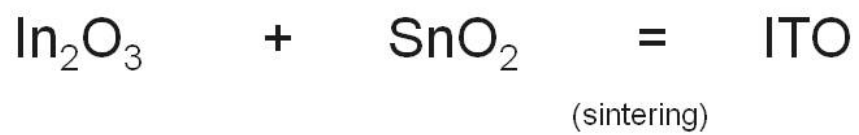
NTP
National Toxicology Program

NTP Research Concept - Indium Tin Oxide (ITO)

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ITO target



ITO nanopowder



Nomination

- NIEHS
- Increased world wide usage
- Lack of adequate toxicity data
- Clinical cases of ITO lung in Japan
- Indium Phosphide (InP) was demonstrated to be carcinogenic in both rats and mice by the NTP in 2001





Production

- 2009 Indium demand = 1555 tons
- 63% generated via 2° production
- 82% used for ITO
- USA imported 150 tons in 2005 compared to 15 tons in 1996

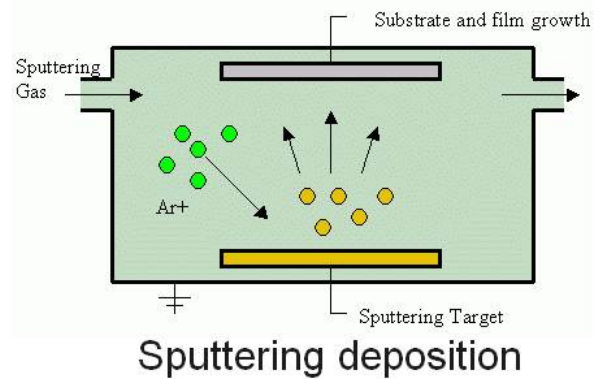
Use

- Thin coating on flat panel displays
- Field emission displays, heat reflective coatings, solar panels, cathode-ray tubes, windows, gas sensors, photovoltaics, windshields and alloys



Human Exposure

- ITO target creation
- ITO film deposition
- ITO recycling
- Planned NIOSH workplace survey
 - ACGIH TLV: 0.1mg/m³ TWA for In₂O₃
 - NIOSH REL: 0.1 mg/m³ for In₂O₃; 2mg/m³ for SnO₂
 - Indium exposure limit set using unsintered In₂O₃ data





ITO Exposure in the Scientific Literature

Clinical cases of indium lung (ITO) in Japan

- Interstitial pneumonia, two cases of fatal pneumothorax, fibrous lung tissue, interstitial changes on HRCT, elevated serum indium and KL-6 levels

Animal data

- Single **ITO** intratracheal administration in female Wistar rats
- Weekly **ITO** and **InP** intratracheal administration in hamsters
- Single **ITO** oropharyngeal administration in B6C3F1 mice

Sintered versus unsintered Indium compounds

- Sintered ITO more toxic than equivalent mix of unsintered IO and TO
- Sintering may enhance toxicity of indium compounds by increasing solubility



Indium Phosphide Inhalation



Assumption 1:
Biological Processing
by lung macrophages?

Free Indium in lung?



Assumption 2:
Free indium causes cancer?



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Chemistry
Tissue ICP-MS

Soluble Indium comparative studies



Key Issues

- Issue 1: Solubility of Indium Compounds
- Issue 2: Sintered vs. non-sintered ITO
- Issue 3: Particle size
- Issue 4: Developmental and reproductive toxicology of Indium compounds
- Issue 5: ITO carcinogenicity potential
- Issue 6: Carcinogenic potential of free indium



Proposed Approach and Specific Aims

- *Tier 1: Chemistry of indium compounds*
 - Specific Aim 1: Determine the relative solubility of indium compounds
- *Tier 2: 14-day, 90-day subchronic and DART inhalation exposures*
 - Specific Aim 2: Assess ITO and indium chloride toxicity in subchronic studies
 - Specific Aim 3: Assess indium compound effects on reproduction and development if necessary
- *Tier 3: Chronic inhalation exposure*
 - Specific Aim 4: Assess long-term toxicity of ITO and indium chloride



Significance and Expected Outcomes

- NTP studies on ITO and InCl_3 will
 - Address solubility of indium compounds
 - Characterize ITO toxicity and potential carcinogenicity in both rats and mice following inhalation exposure
 - Provide data for use in setting occupational exposure limits
 - Allow some form of comparison between ITO, InCl_3 and InP toxicity
 - May allow similar regulation of all indium compounds